

Here is the link to the Wiki page:

<http://spl-work-group.wikispaces.com/>

Topics/Questions for Discussion for SPL ER/DL Process Team – 26-Jul-17

Email Clean Up

If someone needs to be added back on, please have them reach out to both Herb and I:

Benjamin.E.Harpster@gsk.com

Herbert.Obrien@bayer.com

SPL Jamboree

Who will be attending?

A separate e-mail will be sent with information regarding the hotel reservations and the ice-breaker. Please respond to Virginia if you plan on reserving a room.

Output from SPL Working Group Leadership Team 22-Jun-17

- A. Change from "...manufactured exclusively for private label distributor" to "...manufactured under contract" marketing categories transition/deprecation timeframe.
- For these, NDCs often used for imports only. The SPLs are not usually publicly available, and are not released except through FOIA requests.
 - Approved Drug, OTC drug categories. These phrases were originally intended for private label manufacturing; however, there are multiple instances where the manufacturing is done for non-private label manufacturers. Terminology has been available since March 2017. At some point the old terms should be removed.
 - The FDA has already published the new terms in the thesaurus and mentioned in the implementation guide. Impact on the vendors: the implementation guide is already published with the new terminology; the vendors need to roll out any changes within their tools. The published implementation guide reflects the changes to the system at the FDA.
- B. SPL stylesheet updates during second half of 2017. Expect multiple stylesheet updates between now and the end of 2017.
- This does not appear to be a major impact on the vendors, as many use a single URL to connect through to the stylesheet(s).
 - This single URL has cascading stylesheets underneath.
- C. "Chewable Gel" dosage form & NCI concept code. This new term is to be used for 'substances are usually those typically used in formulating a 'gummy' product'.
- One example of a product that would now use this 'Tums Chewy Delights' [GSK]
- D. Conversion from "http" to "https" stylesheet and schema references in SPL files transition/deprecation - validation timeframe.

- This change was required by the White House via Executive Order, with an implementation date of December 2016. Accessdata – which holds the stylesheets -- has now made this change, and stylesheets can now be updated.
- NLM is in scope of this requirement, as well.

SPL @ HealthCanada

- HealthCanada has announced the beginning of a Structured Product Monograph pilot.
- For more information, the contact for the SPM initiative through Health Canada is Craig Anderson, who is the project lead. His email address is craig.anderson3@canada.ca.
- Marcia has reached out to her counterpart in Canada; if there is interest, they will be attending Process ER/DL team and/or Leadership Team at some point in the future. I have attached the letter for those interested in the pilot.

Members Questions

1. From Amanda Broughton at Jubilant HollisterStier

“Federal Register, Aug. 31, 2016 (Vol. 81 No. 169) – Clarification on the CMO obligation to list drugs under own manufacturer labeler code.” My company manufactures product as a CMO for many clients, whom all register their own products under their own labeler codes (because they are the license holders and maintain the labeling).

How would I go about listing these drugs without providing any labeling info to FDA that they are already receiving via the client’s SPL drug listing?

Here is what I put in the manufacturer drug listing:

- The PDP section using the commercial label for finished goods and the bulk label for bulks. The Product Data Elements section:
- For **bulk**, it should contain the product information (example, for tablets, it should have all the same ingredients and attributes). Also, it should show what you are shipping.
- If you are sending 10,000 tablets in a drum, that that should be the packaging description. And for the category, I put “bulk for further processing”.
- If, however, you are making the **packaged finished good**, then the Product Data Elements should exactly match the client’s information except for 2 things. First, the NDCs will need to use a Labeler code specific to your company. Second, for the category, you would use “Approved Drug Product Manufactured Exclusively for Private Label Distributer” (the wording for this is going to be changing in the future).
- There is an OTC specific version of this also. In the Labeler/Manufacturer section, it should contain your information for the labeler code used and I only list my manufacturing sites.
- Others may add more detail here.

- Also, I do separate listings for each manufacturing site, even if they are making the same product. I do not believe this is required; I do it so that the labeler code that I use is specific to the site in question. Personal preference. **Ben Harpster**
- The company that packages the drug and puts it into final form is the one that uses the Approved Drug Product Manufactured Under Contract or Exclusively for Private Label Distributor marketing category. That packager has the responsibility to list the distributor drug because they manufacture the finished product. If the distributor is sent the product in bulk and they send it to the market. The final packager is regarded as the one who is manufacturing under contract. **Howard Shatz**
- The manufacturer is required. Someone has to do the distributor drug listing whether it is the packager, manufacturer, or distributor themselves. But the manufacturer has to have a listing too. **Ben Harpster**
- Paul L stated that the one who manufactures the drug but doesn't package it is just drug for further processing. The one who is manufacturing the product for the distributor is the packager and the packager would be responsible for the listing. The distributor is welcome to do the listing but if they do not, the FDA will hold the manufacture responsible. **Howard Shatz**
- Please check what the FDA's definition of what a Manufacturer is, if you are just manufacturing product, you are considered a manufacturer. If you are only packaging a finished product, you are also considered a manufacturer.
- All that they want in SPL is the Manufacturer and the Distributor/the Labeler which could be the manufacturer or the distributor and then you list all of the manufacturing sites. A company that is only an NDA holder is represented in the SPL by the NDA Number, their names and DUNS number are not there and they have no responsibility for listing.
- Even if the distributor does the listing the manufacturer needs to do a separate listing.
- Unless they are under your corporate umbrella, then you are not required to do the manufacturer listing but it is recommended. If this is not done, you will need to explain the relationship between the 2 companies with every shipment.
- The distributor needs to supply the manufacturer with the information for their drug listing, recommend to add the drug listing as part of the agreement with the manufacturer that will show who is responsible for the listing and for the contract manufacturer to provide proof of the listing.
- Nothing is allowed for interstate commerce if the listings are not in place. There can be 2 or more NDC numbers for a drug including the API, bulk drug, packager, distributor to track the steps in the drug supply and to track the different sites to make sure they are being inspected routinely.
- The manufacturer needs to be aware that they are providing drugs for the US market.
- The different types of drug listings populate the database that the FDA officers at the ports of entry use to verify their information.
- The packer or repacker drug listing in the CoL doesn't alleviate them from their own listing.
- Some distributors choose to do the manufacturers listings for their foreign manufacturers, some manufacturers do the listings for the distributor as well as their own listing, some manufacturers do

only their listing and the distributors do their listing. This is based on your agreement with the manufacturer.

- In the past the distributor who would do the listing for the manufacturer, they were able to claim confidentiality of their contract manufacturer. What happens if the manufacturer is going to list and post a label image?
 - The manufacturer posting does not become public knowledge it is for internal FDA Databases
 - The commercial listing is what appears on the DailyMed
 - For OTCs, the distributor drug lists their product and a contract manufacturer image is included, it is because they did not use the correct category. Drugs for further processing or private label distributor do not appear on the DailyMed.
2. The regulation reads that the repackager has to list the product. If you are getting in a product from the manufacturer with one NDC and repackaging it for a private labeler NDC, what NDC do you assign to it?
- They are not a repackager in that case, they are getting it in bulk. They are a packager and have to have their own labeler code and assign an NDC code for that product. And they list as manufactured under contract.
 - If they are putting it into packages and it goes to another company that does the labeling that company would be manufacturers under contract and the company that just packages it is drugs for further processing.
 - There has to be a drug listing for each step. The bulk manufacturer has to list, the packager has to list, the labeler has to list and the distributor has to list. **Howard Shatz**
3. Is there a special code for a manufacturer listing compared to a commercial listing?
- For bulk products you use the bulk style sheet
 - If you are doing manufactured from a private label distributor, use an OTC or Pharma template and assign the categories in the product data elements for private label distributor to create the listing.
 - If what you are producing is not in final packaging it would be drugs for further processing. The Bulk ingredient is for an API.
 - If you are making finished goods for the US and also produce a bulk product to be shipped overseas for further packaging, they need to have different NDC numbers to populate the systems properly. The bulk would be for export only.
4. From Amanda Broughton at Jubilant Hollister Stier

Process for De-Registering an NDC – SPL vs. NDC Database Discrepancy - If a company files a market end date to their drug listing, does this automatically update the NDC database?

- This was my understanding, but not until the market end dates have passed. *Anyone else had a different experience?*
- Specifically, my company ended the drug listing a set of diluents manufactured under DMF back in 2009, per FDA request since the diluents do not contain active ingredients

- Further research has shown that they were not removed electronically.
- With serialization implementation, we want to be sure we have a solid understanding of whether these products require it, considering FDA has told us in the past they didn't require NDC #'s and to de-list them. We have a similar question on some Sterile Empty Vials we also manufacture under a Type II DMF that do not have an SPL drug listing.

- Under the Product Data Elements, simply change the “Marketing Status” to “Completed” and then enter in a “Marketing End Date”. The Marketing End Date is the date you no longer plan to market the product. Save and then create a new submission to send to the FDA indicating that this product is to be delisted. This is also the date that it will be archived on the Daily Med.

- If you are trying to delist an older R3 product that is on the Daily Med, you will need to create a new submission file and update it to R4. When you enter the information for the Manufactured product, enter in a marketing start date (the day you started marketing the product to the public) AND a marketing end date (the date you plan to stop marketing this product). Create the submission files as normal and then submit to the FDA.
- If this product has been discontinued for a long amount of time or you genuinely cannot find a principal display panel, you may create your own image with the words “Product Discontinued” prominently displayed and use it as the principal display panel. This is only to be used if you cannot find the principal display panel.

- Establishments will not be required by the SPL Portal validation logic when all associated manufactured products have a status of “Complete” and a date populated in the “Marketing End Date” field.
- FDA Serialization Guidance
<https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM206075.pdf>
- Serialization DCSA update... In brief, FDA does not intend to take action against manufacturers who do not affix or imprint a product identifier to each package and homogenous case of products intended to be introduced in a transaction into commerce before November 26, 2018. This represents a one year delay in enforcement of the requirement for manufacturers to affix or imprint product identifiers. For the products that manufacturers introduce in a transaction into commerce before November 26, 2018, without a product identifier, FDA also does not intend to take action against manufacturers who do not use a product identifier to verify such product at the package level.

Herb Obrien <http://www.splportal.com/help/NetHelp/index.html#!Documents/howdoidelistoneofourproducts.htm>

5. Are companies putting the diluents in the drug listings if they contain no drugs?
 - For kits, you do not need to include the diluent
 - For a kit the inner pieces of a kit do not have the same product code
 - The drug product needs to have it's own product code separate from the kit
 - The diluent is listed as a component of the kit but does not have it's own NDC since a diluent is not a drug.
 - CBER requires an NDC assigned to every level of packaging
 - For Biologics, the diluent is listed as part 2 of the kit, sterile water, inactive ingredients, vial and is assigned it's own NDC. The product code is unique so it can be used for multiple products.

QUANTITY OF PARTS		Select Part Type:	Drug part	
Part #	Total Product Quantity	Remove		
Part 1	2.5			
Part 2	2.5			
+ Part 1 of 2 (Drug Part)				
BRAND NAME	Kovaltry	SUFFIX	GENERIC NAME Antihemophilic Factor (Recombinant)	
- Part 2 of 2 (Drug Part)				
BRAND NAME	diluent	SUFFIX	GENERIC NAME water	
Dosage Form	SOLUTION		Source Product Code	
Route Of Administration	INTRAVENOUS		DEA Schedule	
- INGREDIENTS				
Name (Active Moiety)	Type	Strength	Remove	
WATER	Inactive			
+ PRODUCT CHARACTERISTICS				
- PACKAGING				
#	NDC	Package Description	Package Details	
1	0026-0426-02	2.5 mL In 1 SYRINGE		

6. How have people removing diluents from drug listings if requested to do so?

- What takes a product off of the NDC Database?
- I thought if the drug listing was updated it would be removed
- There are marketing start and end dates on the NDC level and the product level. If you only put it on the NDC level and leave it off the product level, it will not archive your file. NDC directory is using an algorithm and the end dates that are reflected there are for the product level not the NDC specific end dates.
- If the end dates are on the NDC level and not on product level, the NDC database would not be updated.
- To de-list the product as a whole, it must be delisted on all layers. If delisting one packs size, it needs to be on the full pack size. The NDC directory will be updated once that date passes.

7. Frances Change from Amgen

We have a Kit that contains a vial of drug product + syringe of diluent. The drug product vial is not marketed by itself, but as a part of the kit. The drug product vial has the same NDC product code as the Kit. As part of drug listing process, we are not able to drug-list the product itself because it is part of the Kit. Our drug product vial is unable to be imported into the country because customs cannot associate the NDC number of the vial with the manufacturing site.

Has any other company been faced with this issue? How do they rectify it? Is there a way to drug-list the NDC code of the drug vial component?

- What I believe you are being asked for is a NDC from a manufacturing drug listing. This is how customs and FDA port inspectors verify/connect product made and manufacturer. The manufacturer has the responsibility to drug list, though the distributor could perform it for them. Either way, the labeler code has to be specific to the manufacturer.
- Here is an extract from the relevant part of the 21 CFR 207 on who is responsible.
- §207.41 Who must list drugs and what drugs must they list?
 - Each registrant must list each drug that it manufactures, repacks, relabels, or salvages for commercial distribution. Each domestic registrant must list each such drug regardless of whether the drug enters interstate commerce. When operations are conducted at more than one establishment, and common ownership and control exists among all the establishments, the parent, subsidiary, or affiliate company may submit listing information for any drug manufactured, repacked, relabeled, or salvaged at any such establishment. A drug manufactured, repacked, or relabeled for private label distribution must be listed in accordance with paragraph (c) of this section.
 - Registrants must provide listing information for each drug in accordance with the listing requirements described in §§207.49, 207.53, and 207.54 that correspond to the activity or activities they engage in for that drug.
- (c)(1) For both animal and human drugs, each registrant must list each drug it manufactures, repacks, or relabels for commercial distribution under the trade name or label of a private label distributor using an NDC that includes such private label distributor's labeler code.
- (2) Additionally, in the case of human drugs, each registrant must list each human drug it manufactures, repacks, or relabels using an NDC that includes the registrant's own labeler code, regardless of whether the drug is commercially distributed under the registrant's own label or trade name or under the label or trade name of a private label distributor.

Debra Goetchius – Janssen

8. We recently had a new product approved and the distribution center in the US wanted to ship product before we received word that the SPL/Drug Listing validation had passed and been posted. We told them that they could not ship until we received confirmation that the SPL was posted. Was this the correct message? If we receive approval, can the product be brought into the US before the SPL has successfully been submitted?
 - Once your SPL passes technical validation you may ship even if it has not yet posted to the DailyMed.
 - GSK does not ship product into the U.S. without having received approval from the FDA for a new product and the drug listing must have passed FDA validation.